Remarks

Reconsideration and withdrawal of the rejections of the claims, in view of the remarks herein, is respectfully requested. Claims 17-19, 32-35, and 38 are amended, and claim 40 is added. Claims 1-30 and 32-40 are now pending in this application.

In response to the finality of the Restriction Requirement, Applicant reserves the right to petition the Commissioner to review the Restriction Requirement.

The Examiner rejected claims 28 and 32-39 under 35 U.S.C. § 112, second paragraph, as being indefinite for the recitation of "specific." This rejection is respectfully traversed.

It is Applicant's position that the metes and bounds of the term "specific" in the phrase "TLR4-specific oligonucleotide" in the context of the claims would be clear to one of ordinary skill in the art. That is, the recited oligonucleotide is one which can anneal to and provide a 3′ end which can prime DNA synthesis of a TLR4 gene and thus is effective to amplify TLR4 DNA, e.g., DNA having SEQ ID NO:62 or its complement. Moreover, the recited oligonucleotide contains nucleotide substitutions useful to detect mutations at particular codons in the TLR4 gene. Evidence that the art worker would understanding the term "specific" in the context of an oligonucleotide is found in Morris et al. (Innovations, 3:1 (1995)), a reference cited against the claims under § 103(a). At page 1 of Morris et al., which relates to directional cloning of cDNA, it is disclosed that sequence-specific primers are used less frequently than oligo d(T) primers in methods to clone cDNAs because sequence-specific primers require some knowledge of the target gene.

Accordingly, the claims are clear and definite. Thus, withdrawal of the § 112(2) rejection is respectfully requested.

The Examiner also rejected claims 28 and 32-39 under 35 U.S.C. § 103(a) as being unpatentable over Rock et al. (Proc. Natl. Acad. Sci. USA, 95:588 (1998)) in view of Morris et al. (Innovations, 3:1 (1995)). This rejection is respectfully traversed.

Rock et al. disclose the cloning of five human Toll-like receptor (TLR) genes. Rock et al. used PCR primers derived from a Toll-like human sequence identified in GenBank to probe a cDNA library to yield a TLR1 cDNA (page 589). It is disclosed that the TLR2-4 genes were cloned by DNA hybridization, and TLR5 is a partial EST sequence (page 589).

Morris et al. teach oligo d(T) primers with linkers containing a restriction endonuclease recognition site, or directional random primers with the linkers, for directional cloning (Figure 1).

The Examiner asserts that it would have been obvious to one of skill in the art at the time the invention was made to practice a method of detecting polymorphisms in human TLR4 through amplification of the nucleic acid with probes comprising restriction sites, given the teaching in Rock et al. to use nucleic acid primers to clone TLR4 genes. The motivation to do so, according to the Examiner, is provided in the Morris reference which teaches that directional random priming using probes comprising restriction sites produces high cloning efficiencies and directionally cloned inserts.

However, neither reference discloses or suggests detecting or determining polymorphisms in amplified TLR4 DNA, much less detecting or determining TLR4 polymorphisms at positions corresponding to residue 299 or 399 of TLR4.

Therefore, withdrawal of the § 103 rejection is appropriate and is respectfully requested.

Conclusion

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney at (612) 373-6959 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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Date March 15, 2005

By _____
Janet E. Embretson
Reg. No. 39,665

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: MS Amendment, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 15 day of March, 2005.

CANDIS BUENDING
Name

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Signature